



Our Ref.: 427.038

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: :
Dennis BIGG et al : Examiner: B. Coleman
Serial No.: 701,893 :
Filed: December 1, 2000 : Group: 1624
For: USE OF... IS INVOLVED :
600 Third Avenue
New York, NY 10016

DECLARATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Christophe Thurieau hereby deposes and says as follows:

That he has been employed by Beaufour Ipsen Group since October 1996 and is the Director of Research of the said company.

That the following tests were conducted under his supervision and he has reviewed the following data which are deemed to accurately reflect the affinity of the compounds according to the present invention on somatostatin receptor(s).

TEST DATA

The affinity of the compounds according to the present invention on human somatostatin receptors have been estimated by measurement of the inhibition of the bond of somatostatin-14 labelled with iodine-125 ([125I-Tyr11]SRIF-14) on the receptors of transfected CHO-K1 cells (Shimon, I. et al. *J. Clin. Invest.* 1997, 99, 789).

The specific bond is obtained by subtracting the non-specific bond (determined in the presence of 0.1 μ M of somatostatin-14)

from the total bond. The results are analyzed by non-linear regression (MDL) and the inhibition constants (K_i) are determined in nM (nanomolar).

CONCLUSION

The results as set forth in the annex ^{show} that the tested compounds have an affinity and a selectivity for the somatostatin receptors.

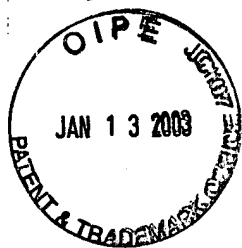
These results confirm that compounds according to the present invention are useful to treat the pathological states or the diseases in which one (or more) of the somatostatin receptors are involved, and preferably to treat acromegalia, hypophyseal adenomas or endocrine gastroenteropancreatic tumors including carcinoid syndrome.

It is declared by the undersigned that all statements made herein of undersigned's own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements made were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S. Code § 1001, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Dated: This day of , 2003.

Christophe Thurieau

CAM:sd



Annex

Ex	Ki (nM)
1	775
2	956
8	257
9	146
10	769
11	1090
13	543
17	328
21	211
22	356
31	145
32	6540
33	606
34	90
35	2835
36	937
39	914
40	2990
42	4823
45	191
46	383
47	123
48	446
49	863
50	1023
52	478
53	207
54	2180
55	700
56	1720